

REMARKS/ARGUMENTS

Claims 1-14 were pending in the above-captioned application. Claim 10 has been amended to more particularly point out and distinctly claim that which Applicants consider to be their invention.

Upon entry of the above-made amendments, therefore, claims 1-14 will be pending in the current application. The amended claims are fully supported in the specification as originally filed (e.g. page 3). The amendments to the Claims do not add new matter. Applicants respectively request that the amendments be entered.

The following remarks, in conjugation with the above amendments, are believed to be fully responsive to the Office Action.

THE REJECTION UNDER 35 U.S.C. § 102 SHOULD BE WITHDRAWN

Claim 10 is rejected under 35 U.S.C. 102(b) as being anticipated by JP 11099192 ("JP '192"). In response, Applicants submit that the rejection should be withdrawn for the reasons stated below.

As noted above, claim 10 has been amended to recite "an organic ligand which forms a coordination complex with the metal". The term "organic ligand" is defined on page 3, lines 24-25 of the specification.

A finding of anticipation under 35 U.S.C 102 requires the disclosure in a single prior art reference of each element of the claim under consideration. *W.L. Core & Associates v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983). There must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention. *Scripps Clinic & Research Found. V. Genetech Inc.*, 927 F.2d 1565, 18 USPQ 2d 1001, 1010 (Fed. Cir. 1991).

The amended claim 10 and the definition of "organic ligand" on page 3, 24-25, make it clear that the chloride ion of JP '192 is outside the scope of the instant invention. Thus, Applicants respectfully submit that the Examiner's rejection under 35 U.S.C. 102 has been overcome and respectfully request that the rejections be withdrawn.

THE REJECTION UNDER 35 U.S.C. 103(a) SHOULD BE WITHDRAWN

Claims 1-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Crane, US Patent No. 5,961,952 ("Crane") in view of JP '192 or Schott Gaswerke, DE 29609958 ("DE '958) or Walther, US Patent No. 6,200,658 ("Walther"). In response, Applicants submit that each of the rejections should be withdrawn for the reasons stated below.

Specifically, the Examiner alleges that "it would have been obvious to one of ordinary skill in the art to modify the compositions disclosed by Crane (i.e., Tc-99m-ligand radiopharmaceutical diagnostic agent) by using vials having a silica coated inside because it known in the art that such vials provide various advantages for the storage of pharmaceuticals, specifically including diagnostic agents and radiopharmaceuticals, as taught by JP '192, DE '958 and Walther, as stated above. One of the ordinary skill in the art would have been motivated to use such improved silica coated vials for the pharmaceutical compositions disclosed by Crane to take advantage of one or all of the advantages taught in the prior art in using such vials for pharmaceuticals, as stated above."

The logic of the Examiner's position is that the person skilled in the art would be motivated to apply any and all improvements which are said to be useful for a given product in the same field. On that basis it would also be obvious to improve all the other elements of the radiopharmaceuticals taught by Crane. Applicants respectfully disagree. Applicants submit that, in reality, the person skilled in the art would inevitably need to exercise judgement as to which specific elements of any prior teaching should be chosen to be improved.

Crane teaches repeatedly (Column 1 lines 62-66, Column 2 lines 33 to 37, Column 3 lines 22 to 26 and Column 3 lines 54 to 59) that three components (a), (b) and (c) are preferred, and thus form important features of the invention:

- (a) a pre-determined quantity of *tertiary*-butyl isonitrile;
- (b) a solubilization aid;
- (c) a pre-determined quantity of a reducing agent.

Applicants submit that the person skilled in the art, even if assumed to be contemplating improvement of Crane, would focus on the repeated teachings in Crane that solubilization aids and reducing agents are important, and be motivated to improve those elements. A logical extension of Crane, where motivation exists would therefore be to seek to employ improved solubilization aids or improved reducing agents. Alternatively, the person skilled in the art could look at feature (a) [*tertiary*-butyl isonitrile], and look to change the ligand to improve performance.

Such improvements all teach away from the present invention. Applicants therefore respectively submit that there is no motivation to change Crane in the specific manner suggested by the Examiner without the application of hindsight (i.e. knowledge of the present invention).

This issue is therefore the selection, i.e. why based on the prior art alone without knowledge of the present invention, the person skilled in the art would be motivated to select to change the vial of Crane, when a whole range of alternatives exist, particularly those options which Crane teaches are important. The following are further responses on the specific document combinations cited by the Examiner.

1. Crane and DE '958

Applicants stress that DE '958 teaches that glass containers having an inner surface coating of oxides or nitrides of silicon, titanium, tantalum and/or aluminum are useful to reduce leaching of impurities from the glass walls into the contents. There is no teaching or suggestion in Crane that the compositions therein suffer from such leaching problems.

Hence, Applicants submit that there would be no motivation for the person skilled in the art to modify Crane in the manner suggested by the Examiner.

Also, DE '958 teaches that a very wide range of oxide or nitride coating materials can be used.

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Also, DE '958 teaches that a very wide range of oxide or nitride coating materials can be used. The combination of Crane and DE '958 therefore logically also gives a wide range of possibilities - it does not lead to the specific teaching of the present claims. Silica is said by DE '958 to be preferred, but the only "diagnostic solution" taught by DE '958 is blood and blood samples. DE '958 provides only a few lines of information, so no further description is supplied. Applicants therefore contend that the person skilled in the art would be unlikely to use DE '958 as a source of teaching on diagnostic agents which are not based on biological fluids or proteins such as blood. Applicants therefore submit that the Examiner's obviousness objection based on this combination of references is invalid, and should be withdrawn.

2. Crane and Walther

The Examiner refers to Column 2 of Walther. Applicants presume that lines 49 to 57 is the section referred to:

"In order to avoid the disadvantages of dealkalizing process it is also known to provide a tubular glass container from low melting glass material, which operates as a packaging device for pharmaceutical materials, having a silicon dioxide (SiO₂) layer

on its interior surface, which has the same inertness as a quartz glass surface (M. Walther, "Packaging of sensitive parenteral drugs in glass containers with a quartz-like surface", in Pharmaceutical Technology Europe, May, 1996, Vol. 8, Nr. 5, pp. 22 to 27."

Applicants stress that Walther is in fact silent on vials, Walther refers to 'hollow glass bodies'. These are described at Column 1 lines 27-41. The Examiner's attention is respectfully drawn to Column 1 lines 20 to 41, where ampoules, bottles, etc are mentioned but not vials. The section of text that the Examiner relies on at Column 2 is in fact unrepresentative of Walther. Thus Walther itself does not limit the nature of the "oxide material" used in the coatings to silica. Even at Column 4 lines 40 to 43, Walther teaches that:

"... the following oxides may be used, among others, as coating materials: SiO₂, Al₂O₃, TiO₂ or mixtures thereof".

Applicants therefore contend that Walther provides no clear teaching that silica is to be used. The combination Crane and Walther in fact leads to a range of possibilities, not just the specific teachings of the present claims. Applicants therefore submit that the obviousness objection based on this combination should be withdrawn.

3. Crane and JP '192

A full English translation of JP '192 is enclosed. The Examiner's attention is drawn to paragraphs [0005] – [0009] and [0024], which address the problem of adsorption of the radiopharmaceutical onto the container wall. The solution provided by JP '192 is to employ silica-coated vials.

Crane, however, specifically teaches "solubilization aids" as a means to overcome such problems – see Column 10 lines 25-35. Solubilization aids are a preferred embodiment of Crane, and are described at:

Column 2 lines 33-47,
Column 3 lines 23-33,
Column 5 line 54 to Column 4 line 2,
Columns 6-9 and 19-22,
Column 7 lines 1-26,
Column 8 lines 33-35

Applicants therefore contend that Crane teaches very clearly that “solubilization aids” are a preferred embodiment and are to be used to overcome any adsorption problems. Therefore Crane teaches very strongly against the combination with JP ‘192 as suggested by the Examiner. Also, since Crane itself already teaches how to solve this problem, applicants contend that the person skilled in the art would not be motivated to seek to solve the same problem again by combining the teaching of JP ‘192 with that of Crane. Applicants therefore submit that the obviousness rejection based on this combination should also be withdrawn.

Thus, Applicants respectfully request that the rejections be withdrawn.

CONCLUSIONS

In view of the amendments and remarks herein, Applicants believe that each ground for rejection or objection made in the instant application has been successfully overcome or obviated, and that all the pending claims are in condition for allowance. Withdrawal of the Examiner's rejections and objections, and allowance of the current application are respectfully requested.

Respectfully submitted,



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